JOC Article

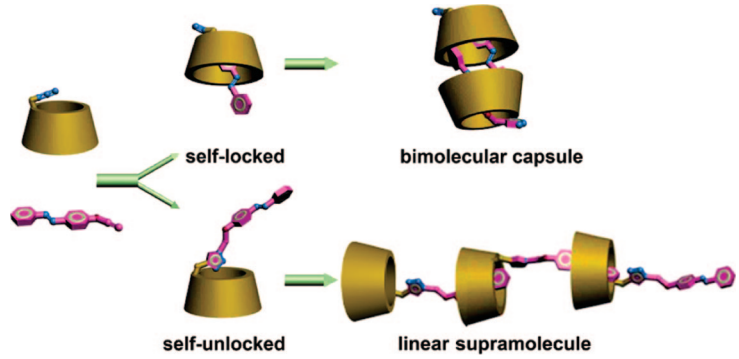
Syntheses and Self-Assembly Behaviors of the Azobenzenyl Modified β-Cyclodextrins Isomers

Yu Liu,* Zi-Xin Yang, and Yong Chen

Department of Chemistry, State Key Laboratory of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, People's Republic of China

yuliu@nankai.edu.cn

Received March 1, 2008



A couple of analogues of azobenzenyl β-cyclodextrins **1** and **2** with self-locked and self-unlocked conformations have been synthesized via the Huisgen cycloaddition from the same reactants, but in distinct reaction conditions (i.e., the hydrothermal synthesis and the "click" reaction, respectively), their conformations were sufficiently proved by X-ray crystal structural analysis, molecular modeling study, and 2D NMR spectroscopy, and their self-assembly behaviors in aqueous solution were also investigated by NMR spectroscopy. Interestingly, the self-locked conformer **1**, which could be regarded as a new type of [1]rotaxane, self-assembled to a novel bimolecular capsule, where its azobenzene substituent was included in both its own cavity and the counterpart's cavity, in aqueous solution and in the solid state. In contrast, by adjusting the conformation of **1** to a self-unlocked one, the resulting conformer **2** was found to self-assemble to a linear supramolecule. These studies have shown the stronger impact of the reaction condition changing in cyclodextrin's modification products and will provide a new access to control the structure of supramolecular assemblies by tuning the conformation of building blocks.

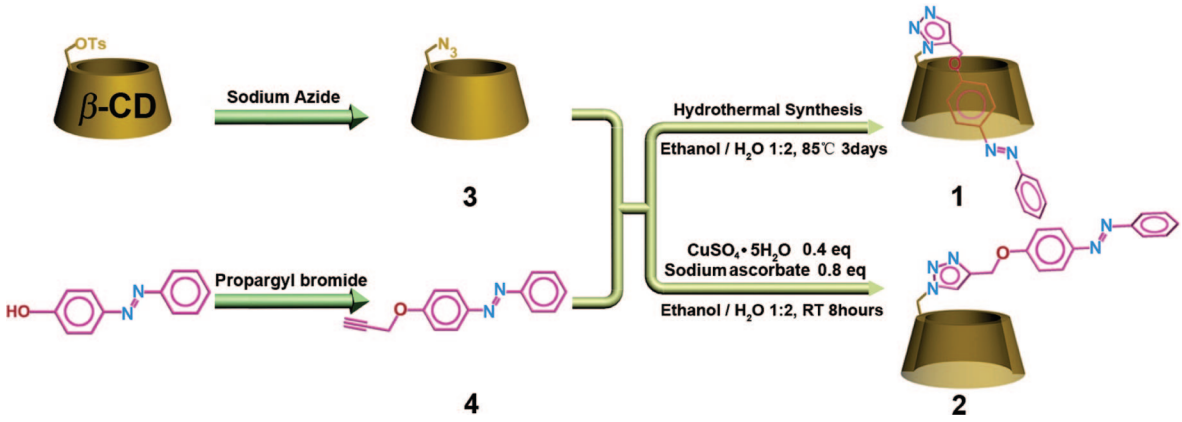
Introduction

The fabrication of nanometer-scaled supramolecular architectures with unique structures and functions is a key aspect in supramolecular chemistry and nanoscience.[1] Possessing the capability of including various organic molecules within their hydrophobic cavities, cyclodextrin (CD) has been used as the basic building block to construct the supramolecular assemblies to study their structure, function, and molecular motion.[2] Superior to those from native CDs, supramolecular architectures constructed from modified CDs with various covalently linked substituents always exhibit more excited functions.[3] In general, there are two assembly modes for modified CDs, that is, the intermolecular inclusion mode and intramolecular inclusion mode. Recently, utilizing the intramolecular inclusion mode of modified CDs, some simple molecular machines with [1]rotaxane or self-included structure have been developed to study the substituent's machine-like movement with the CD cavity.[4] For example, Harada et al. introduced the PEG polymer chain with different lengths or end groups to the CD rim to study their

(1) (a) Tian, H.; Wang, Q.-C. *Chem. Soc. Rev.* **2006**, *35*, 361–374. (b) Balzani, V.; Credi, A.; Silvi, S.; Venturi, M. *Chem. Soc. Rev.* **2006**, *35*, 1135–1179. (c) Saha, S.; Stoddart, J. F. *Chem. Soc. Rev.* **2007**, *36*, 77–92. (d) Lankshear, M. D.; Beer, P. D. *Acc. Chem. Res.* **2007**, *40*, 657–668. (e) Green, J. E.; Choi, J. W.; Boukai, A.; Bunimovich, Y.; Johnston-Halperin, E.; DeIonno, E.; Luo, Y.; Sheriff, B. A.; Xu, K.; Shin, Y. S.; Tseng, H. R.; Stoddart, J. F.; Heath, J. R. *Nature* **2007**, *445*, 414–417. (f) Roithova, J.; Milko, P.; Ricketts, C. L.; Schroder, D.; Besson, T.; Dekoj, V.; Belohradsky, M. *J. Am. Chem. Soc.* **2007**, *129*, 10141–10148. (g) Miljanic, O. S.; Dichtel, W. R.; Khan, S. I.; Mortezaei, S.; Heath, J. R.; Stoddart, J. F. *J. Am. Chem. Soc.* **2007**, *129*, 8236–8246. (h) Guidry, E. N.; Li, J.; Stoddart, J. F.; Grubbs, R. H. *J. Am. Chem. Soc.* **2007**, *129*, 8944–8945. (i) Aucagne, V.; Berna, J.; Crowley, J. D.; Goldup, S. M.; Hanni, K. D.; Leigh, D. A.; Lusby, P. J.; Ronaldson, V. E.; Slawin, A. M. Z.; Viterisi, A.; Walker, D. B. *J. Am. Chem. Soc.* **2007**, *129*, 11950–11963. (j) Frampton, M. J.; Anderson, H. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 1028–1064.

10.1021/jo800488f CCC: $40.75
Published on Web 06/13/2008

SCHEME 1. Syntheses of 1 and 2



self-threading and self-dethreading dynamics as well as the thermal or photochemical control of conformational exchange of substituents.[5] Easton et al. constituted a molecular machine from modified CDs, and the photoisomerization of its substitutent changed the in/out conformation of CD and provided the on/off switch of the machine.[6] On the other hand, the intermolecular inclusion mode of modified CDs was reported to result in the formation of complicated assemblies, such as a hermaphrodite [2]rotaxane with a daisy chain structure[7] and supramolecular polymers through host−guest interactions.[8] However, these studies were mainly focused on the assembly behaviors of modified CDs with either self-included or self-excluded conformation; the comparative study on the self-assembly of modified CDs with the same composition but disparate conformations is still rare, to the best of our knowledge. In this work, we prepared a couple of azobenzenyl-modified CDs with different topological structures, i.e., a self-locked conformer **1** and its self-unlocked analogue **2**. Significantly, the self-locked **1** presents a structural character of CD-based [1]rotaxane, and this [1]rotaxane self-assembles to a bimolecular capsule in aqueous solution, while its self-unlocked analogue **2** forms a linear supramolecule. It is of our particular interest to elucidate the factors to restrict the conformation of modified CDs and the influences on the self-assembly behaviors of different CD conformers. These studies will serve our deep understanding of the mechanism of supramolecular aggregation and may provide a new way to control the form of supramolecular aggregates by tuning the conformation of building blocks.

Results and Discussion

Synthesis. **1** was synthesized by Huisgen 1,3-dipolar cycloaddition in 69% yield with use of the hydrothermal synthesis (Scheme 1) and easily purified by recrystallization in water, while its self-unlocked analogue **2** was also prepared in 71% yield by "click" chemistry, a Cu^{I}-catalyzed Huisgen 1,3-dipolar cycloaddition. A possible mechanism for the formation of **1** may be that, with the capability of β-CD to include various organic molecules in its hydrophobic cavity, **3** first formed an inclusion complex with the intermediate **4**, and then the reaction between the azido group in **3** and the ethynyl group in **4** gave the product **1**. This procedure is similar to a reported cycloaddition procedure induced by cucurbituril, where a regiospecific 1,4-disubstituted product was obtained through the encapsulation of the cationic substrates in the cavity of cucurbituril.[9] Owing to the steric effect of the CD cavity, the synthesis of the self-locked **1** under hydrothermal condition exhibited good 1,5-disubstituted regioselectivity, like the increase of regioselectivity of nitrile oxide cycloaddition in a β-CD-scaffold.[10] However, it should be noted that the formation of inclusion complex is an equilibrium process, and the formation of self-unlocked isomers of **1** is also possible in the hydrothermal synthesis.

(2) (a) Nepogodiev, S. A.; Stoddart, J. F. *Chem. Rev.* **1998**, *98*, 1959–1976. (b) Wenz, G.; Han, B.-H.; Muller, A. *Chem. Rev.* **2006**, *106*, 782–817. (c) Harada, A. *Acc. Chem. Res.* **2001**, *34*, 456–464. (d) Cheetham, A. G.; Hutchings, M. G.; Claridge, T. D. W.; Anderson, H. L. *Angew. Chem., Int. Ed.* **2006**, *45*, 1596–1599. (e) Michels, J. J.; O'Connell, M. J.; Taylor, P. N.; Wilson, J. S.; Cacialli, F.; Anderson, H. L. *Chem. Eur. J.* **2003**, *9*, 6167–6176. (f) Murakami, H.; Kawabuchi, A.; Matsumoto, R.; Ido, T.; Nakashima, N. *J. Am. Chem. Soc.* **2005**, *127*, 15891–15899. (g) Wang, Q.-C.; Qu, D. H.; Ren, J.; Chen, K.-C.; Tian, H, *Angew. Chem., Int. Ed.* **2004**, *43*, 2661–2665. (h) Qu, D.-H.; Wang, Q.-C.; Tian, H. *Angew. Chem., Int. Ed.* **2005**, *44*, 5296–5299. (i) Park, J. S.; Wilson, J. N.; Hardcastle, K. I.; Bunz, U. H. F.; Srinivasarao, M. *J. Am. Chem. Soc.* **2006**, *128*, 7714–7715. (j) Oshikiri, T.; Takashima, Y.; Yamaguchi, H.; Harada, A. *J. Am. Chem. Soc.* **2005**, *127*, 12186–12187. (k) Onagi, H.; Carrozzini, B.; Cascarano, G. L.; Easton, C. J.; Edwards, A. J.; Lincoln, S. F.; Rae, A. D. *Chem. Eur. J.* **2003**, *9*, 5971–5977.

(3) (a) Nelson, A.; Belitsky, J. M.; Vidal, S.; Joiner, C. S.; Baum, L. G.; Stoddart, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 11914–11922. (b) Ooya, T.; Eguchi, M.; Yui, N. *J. Am. Chem. Soc.* **2003**, *125*, 13016–13017. (c) Liu, Y.; Yu, L.; Chen, Y.; Zhao, Y.-L.; Yang, H. *J. Am. Chem. Soc.* **2007**, *129*, 10656–10657. (d) Liu, Y.; Wang, H.; Chen, Y.; Ke, C.-F.; Liu, M. *J. Am. Chem. Soc.* **2005**, *127*, 657–666. (e) Onagi, H.; Blake, C. J.; Easton, C. J.; Lincoln, S. F. *Chem. Eur. J.* **2003**, *9*, 5978–5988.

(4) (a) Han, Y.; Cheng, K.; Simon, K. A.; Lan, Y.; Sejwal, P.; Luk, Y.-Y. *J. Am. Chem. Soc.* **2006**, *128*, 13913–13920. (b) Deng, W.; Onji, T.; Yamaguchi, H.; Ikeda, N.; Harada, A. *Chem. Commun.* **2006**, 4212–4214. (c) Kuwabara, T.; Shiba, K.; Nakajima, H.; Ozawa, M.; Miyajima, N.; Hosoda, M.; Kuramoto, N.; Suzuki, Y. *J. Phys. Chem. A* **2006**, *110*, 13521–13529. (d) Park, J. W.; Lee, S. Y.; Song, H. J.; Park, K. K. *J. Org. Chem.* **2005**, *70*, 9505–9513. (e) Ma, X.; Qu, D.-H.; Ji, F.-Y.; Wang, Q.-C.; Zhu, L.-L.; Xu, Y.; Tian, H. *Chem. Commun.* **2007**, 1409–1411. (f) Ma, X.; W, Q.-C.; Tian, H. *Tetrahedron lett.* **2007**, *48*, 7112–7116.

(5) (a) Inoue, Y.; Kuad, P.; Okumura, Y.; Takashima, Y.; Yamaguchi, H.; Harada, A. *J. Am. Chem. Soc.* **2007**, *129*, 6396–6397. (b) Inoue, Y.; Miyauchi, M.; Nakajima, H.; Takashima, Y.; Yamaguchi, H.; Harada, A. *J. Am. Chem. Soc.* **2006**, *128*, 8994–8995. (c) Inoue, Y.; Miyauchi, M.; Nakajima, H.; Takashima, Y.; Yamaguchi, H.; Harada, A. *Macromolecules* **2007**, *40*, 3256–3262.

(6) Coulston, R. J.; Onagi, H.; Lincoln, S. F.; Easton, C. J. *J. Am. Chem. Soc.* **2006**, *128*, 14750–14751.

(7) Onagi, H.; Easton, C. J.; Lincoln, S. F. *Org. Lett.* **2001**, *3*, 1041–1044.

(8) (a) Deng, W.; Yamaguchi, H.; Takashima, Y.; Harada, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 5144–5147. (b) Harada, A. *J. Polym. Sci., Part A* **2006**, *44*, 5113–5119. (c) Miyauchi, M.; Hoshino, T.; Yamaguchi, H.; Kamitori, S.; Harada, A. *J. Am. Chem. Soc.* **2005**, *127*, 2034–2035. (d) Liu, Y.; Fan, Z.; Zhang, H.-Y.; Yang, Y.-W.; Ding, F.; Liu, S.-X.; Wu, X.; Wada, T.; Inoue, Y. *J. Org. Chem.* **2003**, *68*, 8345–8352.

(9) (a) Mock, W. L.; Irra, T. A.; Wepsiec, J. P.; Adhya, M. *J. Org. Chem.* **1989**, *54*, 5302–5308. (b) Tuncel, D.; Steinke, J. H. G. *Chem. Commun.* **1999**, 1509–1510. (c) Carlqvist, P.; Maseras, F. *Chem. Commun.* **2007**, 748–750.

(10) (a) Barr, L.; Lincoln, S. F.; Easton, C. J. *Chem. Eur. J.* **2006**, *12*, 8571–8580. (b) Meyer, A. G.; Easton, C. J.; Lincoln, S. F.; Simpson, G. W. *J. Org. Chem.* **1998**, *63*, 9069–9075.

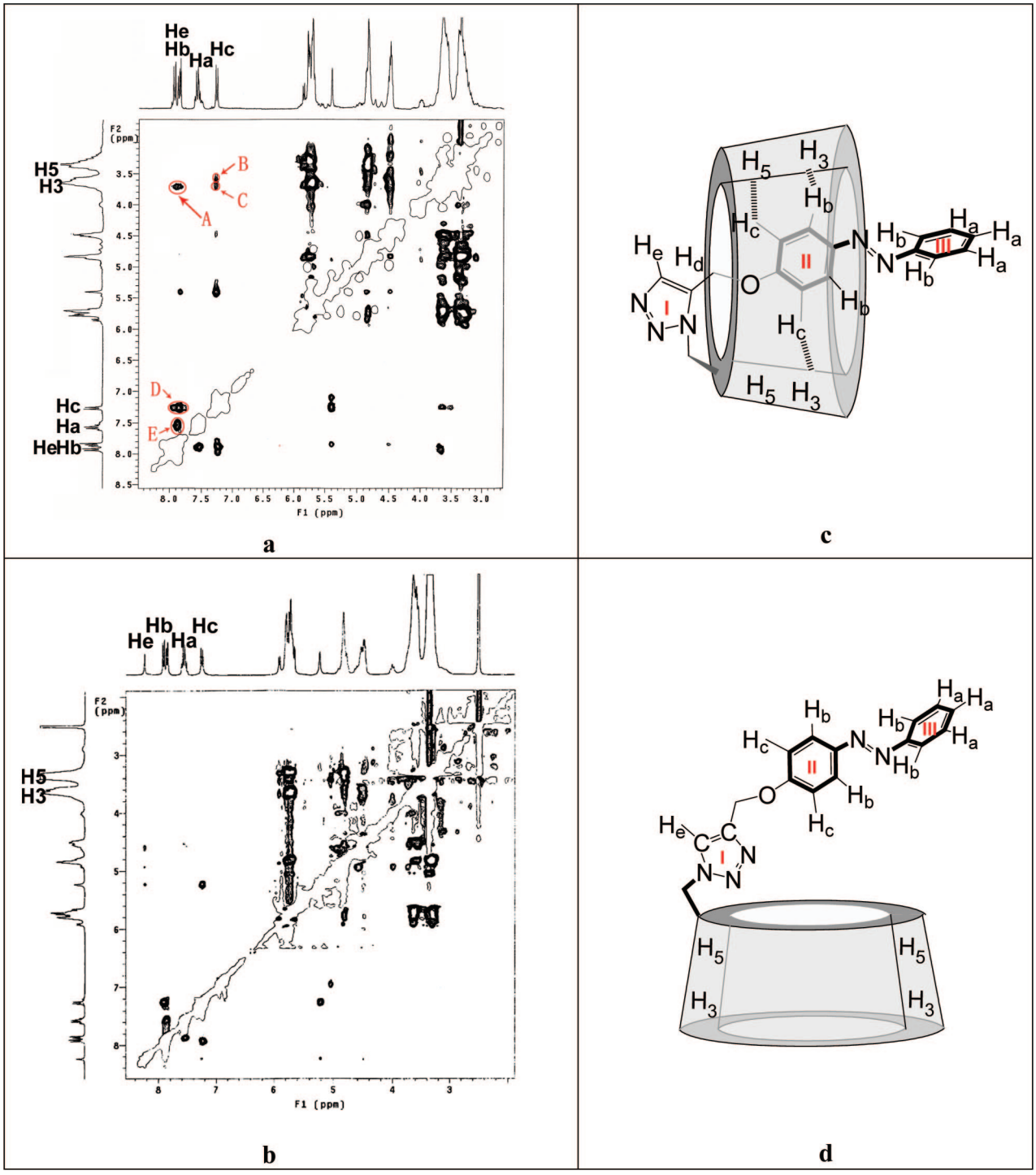


FIGURE 1. ROESY spectrum of (a) **1** (1.9×10^{-3} mol dm^{-3}) and (b) **2** (1.9×10^{-3} mol dm^{-3}) in DMSO-d_6 at 298 K with a mixing time of 300 ms. Possible structures of **1** (c) and **2** (d) in DMSO.

Therefore, we took several methods to avoid, as much as possible, the influence of the isomerization. First, we performed the reaction in water−ethanol solution to maintain the hydrophobic interactions between the β-CD cavity and **4** to some extent. Then, during the purification, the crude products were washed successively with acetone and dissolved in hot water followed by filtration, which would remove the unreacted **4** and possible isomers of **1**, because **4** was soluble in acetone while the possible isomers were poorly soluble in water (control experiments have demonstrated that the water solubility of the self-unlocked **2** obtained from the click reaction was less than 200 μg/mL at room temperature). Finally, because the water solubility of **1** was lower than that of **3**, the unreacted **3** could be efficiently removed by recrystallization. On the other hand, **2** could be easily purified by sufficiently washing the crude product with acetone and hot water to remove the unreacted **3** and **4**.

Structural Analysis of Isomers. The structural analysis of modified CD is very important to understand their molecular assembly behavior. It is well-known that the elucidation of crystal structure is one of the most convincing methods of unequivocally illustrating the geometrical conformation of CD

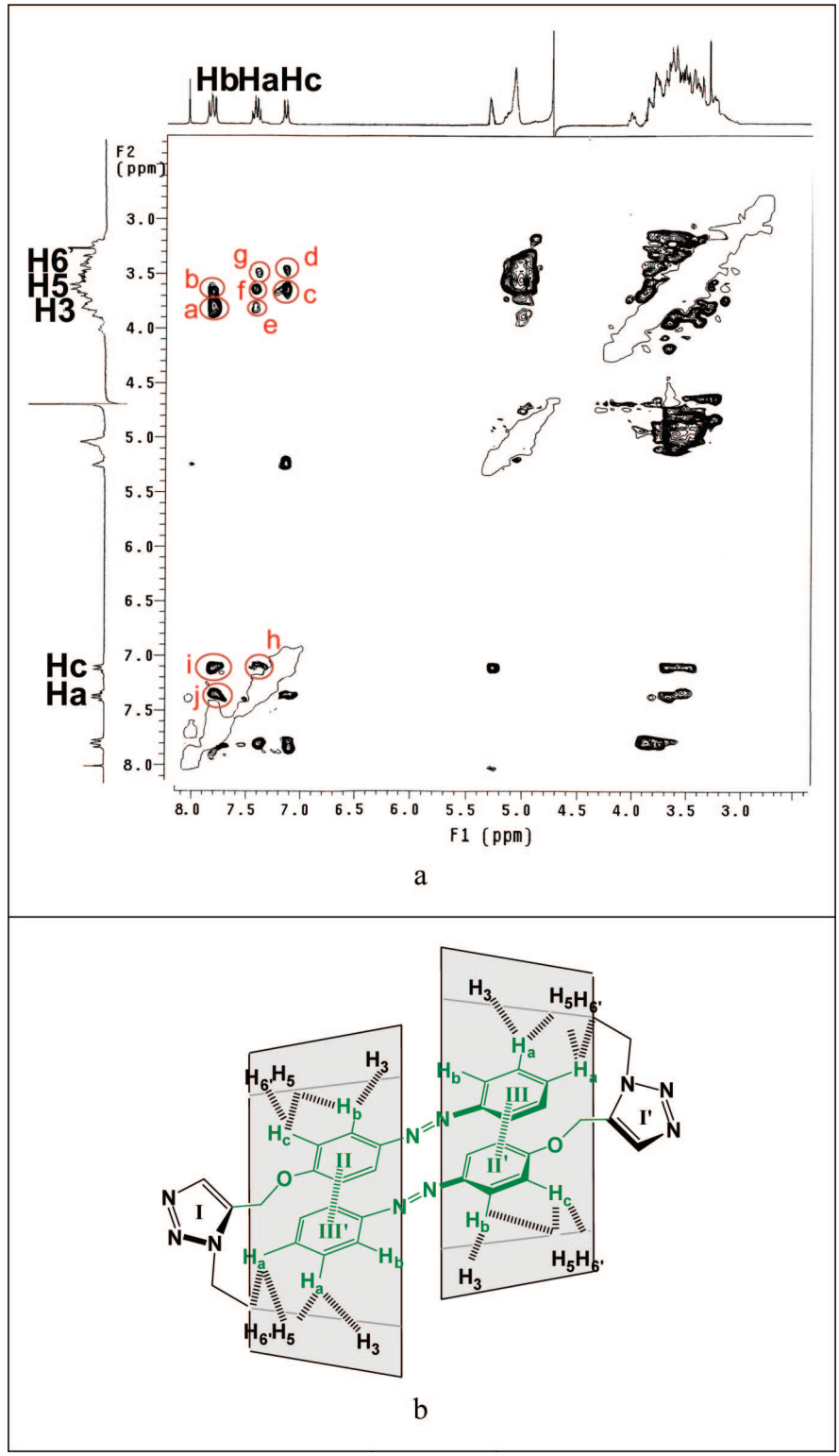


FIGURE 2. ROESY spectrum of (a) **1** (0.9×10^{-3} mol dm^{-3}) in D_2O at 298 K with a mixing time of 300 ms. (b) Possible structure of **1** in water.

derivatives. Unfortunately, our repeated attempts only gave the single crystal of **1** that was suitable for X-ray crystallography. Therefore, we tried to compare the conformations of **1** and **2** through a combinational analysis based on 2D NMR spectroscopy and molecular modeling study. 2D NMR spectroscopy is an efficient method to study the conformation of CD derivatives since one can conclude that two protons are closely located in space (<5 Å) if an NOE cross-peak is detected between the relevant protons in the NOESY or ROESY spectrum. Therefore, it is possible to determine the orientation of the 4-(phenylazo)-phenyloxymethyl[1,2,3]triazolyl substituent related to the β-CD cavity by using the assigned NOE correlations, because if the substituent is self-included in the β-CD cavity, the NOE correlations between the protons of the substituent and the

FIGURE 3. Structural transformation of **1** by changing solvents.

interior protons of β-CD cavity should be observed. A preliminary molecular dynamics simulation study demonstrated that, because the substituent in **1** or **2** had a relatively rigid structure and a longer skeleton length (ca.15.6 Å) than the diameter of the β-CD cavity (6.0−6.5 Å),[11] the conversion between the self-locked conformer and its self-unlocked analogue was unavailable even after increasing the temperature of the system once the substituent was linked to the rigid β-CD rim. Figure 1a illustrated the ROESY spectrum of **1** in DMSO, which displayed the clear NOE correlations between the H3 protons of β-CD and the H_b/H_c protons of the azobenzene moiety (cross-peaks A and C), as well as the NOE correlations between the H5 protons of β-CD and the H_c protons of the azobenzene moiety (cross-peak B). These correlations indicated that the II ring of the substituent was embedded into the β-CD cavity. Moreover, no NOE correlation peaks between the interior protons (H3/H5 protons) of β-CD and the H_a protons of substituent could be found, which indicated that the III ring of the substituent was threaded out of the β-CD cavity. The cross-peaks D and E were assigned to the intramolecular NOE correlations between the H_b protons and the H_c/H_a protons of the azobenzene moiety. In contrast, the ROESY spectrum of **2** showed no appreciable NOE correlations between interior protons of the β-CD cavity and the protons of the substituent, indicating that the substituent group of **2** was entirely located out of the β-CD cavity. According to these NOE signals, we could deduce the possible structures of **1** and **2** as illustrated in parts c and d of Figure 1.

Generally, the [1]rotaxane is defined as a type of supramolecular system consisting of a rod-like molecule (axle component) covalently linking to a cyclic molecule (wheel component), where the axle molecule threads through the cavity of the wheel component, and the wheel component is trapped by bulky ends (stopper) to prevent the unthreading.[2b] On the other hand, it is important to note that CDs were reported to barely include the guest molecule in DMSO due to the solvation and binding of DMSO molecules by CDs,[12] and the exclusion of the self-included substituent of a CD derivative will inevitably take place in a DMSO solution if this conformation conversion is available from the viewpoint of geometry. Therefore, the clear NOE correlations in the ROESY spectrum of **1** in DMSO, along with the molecular modeling study, jointly indicated that **1** could be regarded as a unique [1]rotaxane, although it had no stopper.[3e,4e,f]

Self-Assembly of 1. Interestingly, **1** gave the more complicated NOE signals in aqueous solution than in DMSO. As shown in Figure 2a, besides the NOE correlations (cross-peaks a, b, c, and d) between the H_b/H_c protons of substituent and the $H_3/H_5/H_6$ protons of β-CD, the ROESY spectrum of **1** in D_2O displayed clear NOE correlations (cross-peaks e, f, and g) between the H_a protons of the substituent and the $H_3/H_5/H_6$ protons of β-CD, which were absent in the ROESY spectrum of **1** in DMSO. These correlations indicated that, besides the II ring, the III ring of the substituent, which was located outside the β-CD cavity in DMSO, was also embedded in the β-CD cavity in water. Moreover, Figure 2a also showed a particular NOE correlation (cross-peak h) between the H_a protons and the H_c protons of the substituent that could not be observed in the corresponding ROESY spectrum in DMSO. A simple calculation by MM2 indicated that the distance between the H_a and the H_c protons in a single azobenzene moiety was longer than 5 Å. Therefore, the cross-peak h might not be assigned to an intramolecular NOE correlation, but to the intermolecular NOE correlation between the H_a protons in an azobenzene moiety and the H_c protons in another azobenzene moiety. According to these NOE correlations, we could deduce that the self-locked substituent of **1** may also penetrate into the cavity of another β-CD to form a tail-to-tail bimolecular capsule, where the tail referred to the wide opening of the β-CD cavity, as the possible structure illustrated in Figures 2b. This structural transformation in different solvents was visualized in Figure 3.

Significantly, the tail-to-tail dimer of **1** was also unambiguously verified by the X-ray crystal diffraction in the solid state. The crystal structures were illustrated in Figure 4. As seen in Figure 4a, the 4-(phenylazo)phenyloxymethyl[1,2,3]triazolyl substituent threaded through the β-CD cavity with the II ring of the substituent entirely embedded in the β-CD cavity but the I ring and the III ring located outside the narrow and wide opening of the β-CD cavity, respectively. The much longer distance between the phenyl oxygen and the H-4 atom of the III ring (ca. 11.4 Å) than the inner diameter of the β-CD cavity (6.0−6.5 Å) as well as the rigidity of the substituent linking in the β-CD rim jointly prevented the dethreading of the substituent from the β-CD cavity. These results were in good agreement with the deduced self-locked conformation of **1** in aqueous solution. Figure 4b displayed a clear image of the bimolecular capsule of **1** in the solid state. It should be noticed that the bimolecular capsule in aqueous solution is more compact than that in solid. Further investigations showed that there existed several types of intramolecular and intermolecular interactions within the bimolecular capsule. The intramolecular interactions contained a C−H$\cdots\pi$ interaction (d = 2.810 and 2.638 Å for two units of **1**) between the C-6 atom of β-CD and the I ring of substituent and six hydrogen bond interactions between the O-2 atom of each glucose unit and the O-3 atom of the adjacent glucose unit (O$\cdots$O distance 2.7−3.2 Å), while the intermolecular interactions included a hydrogen bond between the hydroxyl groups on the wide opening of the counterpart β-CD (O$\cdots$O distance 2.745 Å) and two $\pi-\pi$ interactions between the II (III) ring and the III′ (II′) ring in a face-to-face arrangement of two substituents (centroid distance: II ring−III′ ring 3.816 Å, III ring−II′ ring 3.922 Å). These interactions jointly stabilized the capsule-like structure of **1**.

It is well-documented that there exist four crystal structures of monomodified CDs based on the spatial relationship between the substituent and the CD cavity.[13] The first one is the self-included type, where the substituent is included in its own cavity. The second is the layer type, where the substituent is located out of any CD cavity. The third is the mutual-locked dimer type

(11) Szejtli, J. *Chem. Rev.* **1998**, *98*, 1743–1754.

(12) (a) Fujita, K.; Ueda, T.; Imoto, T.; Tabushi, I.; Toh, N.; Koga, T. *Bioorg. Chem.* **1982**, *11*, 72–84. (b) Liu, Y.; Zhao, Y.-L.; Zhang, H.-Y.; Fan, Z.; Wen, G.-D.; Ding, F. *J. Phys. Chem. B* **2004**, *108*, 8836–8843. (c) Shikata, T.; Takahashi, R.; Onji, T.; Satokawa, Y.; Harada, A. *J. Phys. Chem. B* **2006**, *110*, 18112–18114.

(13) (a) Harata, K.; Takenaka, Y.; Yoshida, N. *J. Chem. Soc., Perkin Trans.* **2001**, *2*, 1667–1673. (b) Lindner, H. J.; Yuan, D.-Q.; Fujita, K.; Kubo, K.; Lichtenthaler, F. W. *Chem. Commun.* **2003**, 1730–1731.

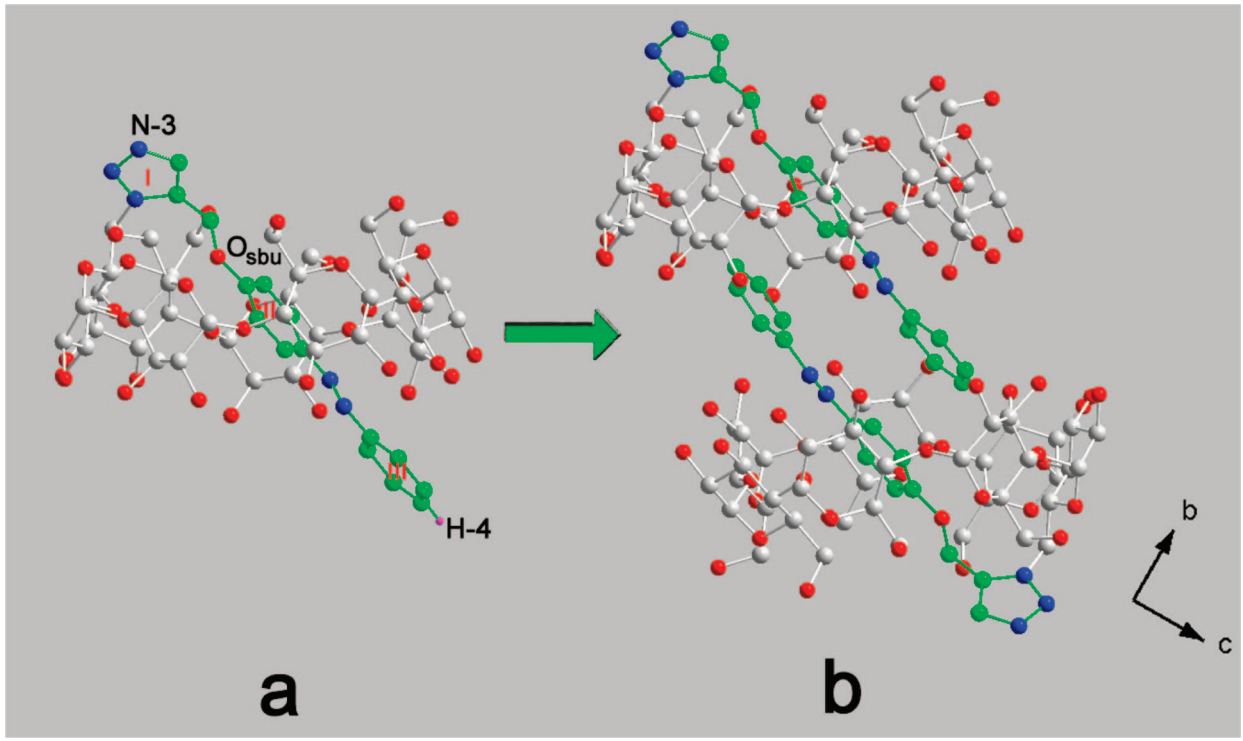


FIGURE 4. (a) X-ray crystal structure of **1** with H atoms and solvent water molecules omitted for clarity; the molecules are colored by atom type: green, carbon atoms in the substituent; gray, carbon atoms in the β-CD; red, oxygen atoms; and blue, nitrogen atoms. (b) Stereodrawing of the structure of the bimolecular capsule.

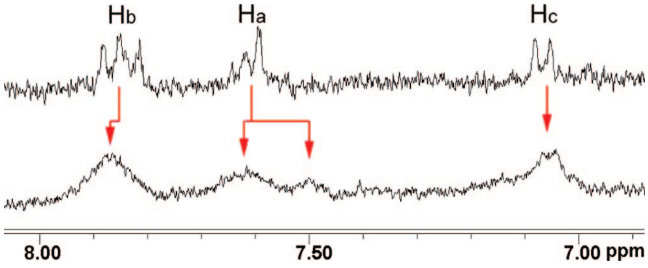


FIGURE 5. Partial ^{1}H NMR spectra of **2** (bottom) and **4** (top) in D_2O-DMSO-d_6 (v:v = 9:1) at 298 K with DSS as the standard.

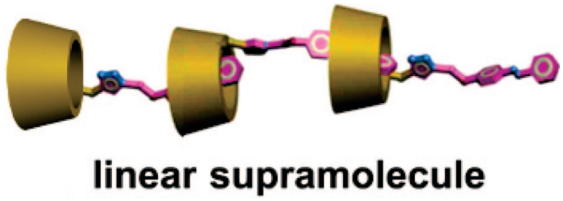


FIGURE 6. Possible self-assembly structure of **2**.

(the "yin−yang" type), where a CD dimer is formed with the modified rims closely located, and the substituents are accommodated in each other's cavities. The fourth, which is frequently observed in the CD crystals, is the channel type, where the substituent of a modified CD unit penetrates in the cavity of the adjacent CD unit to form a polymeric supramolecule. Interestingly, the self-assembly structure of **1** was found to not belong to any of the above types, because its azobenzene substituent was included in both its own cavity and the counterpart's cavity.

Self-Assembly of 2. Because of its poor water solubility, the self-assembly behavior of **2** in water is difficult to investigate by using the ROESY spectrum even in the presence of 10% DMSO. However, a comparison of the ^{1}H NMR spectra of **2** and **4** in D_2O−DMSO (v:v = 9:1) solution still gave useful information about the assembly behavior of **2**. As shown in Figure 5, the δ value of the H_a protons of **2** showed a clear broadened and upfield shift (ca. 0.1 ppm), while those of H_b and H_c protons showed no appreciable shift, as compared with the corresponding protons of **4**.

Generally, the chemical shift values of the guest protons tend to show appreciable changes if the guest molecules are included in the CD cavities.[14] Therefore, Figure 6 indicated that the III ring of the substituent moiety of **2** partly entered the CD cavity. Considering the self-unlocked structural feature of **2**, where the substituent was located out of its own β-CD cavity, we could deduce that the III ring of **2** shallowly penetrated into the cavity of an adjacent β-CD. But there may exist two possible self-assembly modes of **2**: a linear aggregation or a dimer with mutual-insertion from the first face of the β-CD cavity. The FTICR-MS (Fourier Transform Ion Cyclotron Resonance Mass Spectrometry) of **2** clearly showed the peak of $[3M_2 + K + H]^{2+}$ (2114.18). Judging from the structural feature of **2**, the formation of the $3M_2$ aggregate indicated that the aromatic substituent of **2** must be intermolecularly included into the hydrophobic cavity of another β-CD from the secondary hydroxyl side. According to this intermolecular inclusion mode, the formation of the linear supramolecule of **2** in the solid state should be a natural process,[15] although the existence of the dimeric structure could not be rigorously ruled out. Just as many aromatic modified CDs which have been demonstrated to form the linear supramolecules (channel aggregations) in aqueous

(14) Schneider, H.-J.; Hacket, F.; Rudiger, V.; Ikeda, H. *Chem. Rev.* **1998**, *98*, 1755–1786.
(15) Liu, Y.; Fan, Z.; Zhang, H.-Y.; Diao, C.-H. *Org. Lett.* **2003**, *5*, 251–254.

solution and the solid state,[8d,15,16] the self-unlocked **2** showed many appropriate linear aggregations in its high-resolution TEM image (see the Supporting Information) And the XRD of **2** exhibited a strong peak at $2\theta = 18.380°$ ($d = 4.8230$ Å, $I/I_0 = 100$), which was reported to be a characteristic peak of channel packing of CDs.[17]

Conclusions

In summary, a couple of modified β-CD analogues with a long and rigid substituent have been designed and synthesized via the Huisgen cycloaddition in either the hydrothermal synthesis condition or the "click" reaction condition and present the distinct topological structure as self-locked or self-unlocked. The self-locked **1** has a novel [1]rotaxane structure without the stopper part. Interestingly, this [1]rotaxane self-assembles to a unique bimolecular capsule. In contrast, its self-unlocked analogue **2** exhibits a linear supramolecular structure. This is a rare report on the differently restricted conformation of modified CDs with the same composition, and these new observations show clearly the influence of the conformational factors on the self-assembly behaviors of modified CDs. These results will be useful for our deep understanding of the supramolecular aggregation phenomena, and may open a new way to obtain the versatile materials from the controlled supramolecular self-assembly.

Experimental Section

Synthesis of 4-Propargylazobenzene (4). To a solution of acetone (30 mL) containing 4-hydroxyazobenzene (1.0 g) and NaH (0.5 g) was added propargyl bromide (2.5 mL), and the resulting mixture was stirred at room temperature for 3 h. The solvent was removed under reduced pressure, and the residue was recrystallized from petroleum ether to give **4** (0.9 g, yield 75%) as a salmon pink crystall. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.80−8.00 (m, 4H, H of Ph), 7.40−7.60 (m, 3H, H of Ph), 7.10−7.15 (m, 2H, H of Ph), 4.77−4.78 (d, 2H, H of methylene), 2.56 (t, 1H, H of alkyne). ESI-MS *m/z* 259.14 ($M + Na^+$).

Synthesis of Mono-6-deoxy-6-{5-[(*E*)-4-(phenylazo)phenyloxymethyl][1,2,3]triazolyl}-β-CD (1). 3 (0.58 g) and **4** (0.14 g) were dispersed in a water−ethanol solution (12 mL, v:v = 2:1), and the resulting mixture was stirred for 8 h. Then, the turbid solution was put in a Teflon-lined stainless bomb, which was sealed and then heated at 358 K under hydrothermal conditions for 3 days. When the solution was cooled to room temperature, orange-red crystals available for X-ray crystallography were obtained. The crystals were collected by filtration and washed with acetone (3 × 50 mL), and then recrystallized from boiling water. The precipitate was collected by filtration to give **1** (0.48 g, yield 69%). ^{1}H NMR (300 MHz, DMSO-d_6, ppm) δ 7.80−8.00 (m, 5H, H of alkene and Ph), 7.45−7.65 (m, 3H, H of Ph), 7.20−7.30 (m, 2H, H of Ph), 5.60−6.00 (m, 14H, O-2,3 H of β-CD), 5.40 (d, 2H, H of methylene), 4.76−4.90 (s, 7H, C-1 H of β-CD), 4.40−4.66 (m, 6H, O-6 H of β-CD), 3.00−4.00 (m, 42H, C-2, C-3, C-4, C-5, C-6 H of β-CD). ESI-MS *m/z* 1396.38 ($M + H^+$), 1418.53 ($M + Na^+$). Elemental Anal. Calcd for $C_{57}H_{81}O_{35}N_5 \cdot 8H_2O$: C 44.44, H 6.35, N 4.55. Found: C 44.57, H 6.34, N 4.41.

Crystal data for **1**: $C_{114}H_{224}N_{10}O_{101}$, $M = 3351.03$, monoclinic, space group $P2_1$, $a = 15.6068(19)$ Å, $b = 20.806(3)$ Å, $c = 23.361(3)$ Å, $\alpha = 90°$, $\beta = 91.114(2)°$, $\gamma = 90°$, $V = 7584.4(16)$ Å^3, $Z = 2$, $D_c = 1.467$ g·cm^{-3}, λ(Mo−Kα) = 0.71070 Å, $T = 113(2)$ K, $F(000) = 3572$, $\mu = 0.130$ mm^{-1}, approximate crystal dimensions 0.32 × 0.28 × 0.26 mm^3, θ range = 1.30−26.00°, reflections collected/unique 82797/28740 ($R_{int} = 0.0605$), final R indices [$I > 2\sigma(I)$] $R_1 = 0.0763$, $wR_2 = 0.2010$, R indices (all data): $R_1 = 0.0826$, $wR_2 = 0.2079$, goodness of fit on $F^2 = 1.033$.

Synthesis of Mono-6-deoxy-6-{4-[(*E*)-4-(phenylazo)phenyloxymethyl][1,2,3]triazolyl}-β-CD (2). 3 (0.58 g) and **4** (0.14 g) were dispersed in a water−ethanol solution (12 mL, v:v = 2:1), and sodium ascorbate (0.08 g) and $CuSO_4 \cdot 5H_2O$ (0.05 g) were added. The resulting mixture was stirred at room temperature for 8 h. The solvent was removed under reduced pressure, and the residue was washed with acetone (3 × 100 mL), 15% ammonia (3 × 10 mL), and hot water (3 × 40 mL), then dried in vacuum to give **4** as a yellow powder (0.50 g, yield 71%). ^{1}H NMR (300 MHz, DMSO-d_6, ppm) δ 8.21 (s, 1H, H of alkene), 7.80−7.95 (m, 4H, H of Ph), 7.48−7.60 (m, 3H, H of Ph), 7.18−7.30 (m, 2H, H of Ph), 5.58−6.00 (m, 14H, O-2,3 H of β-CD), 5.20 (d, 2H, H of methylene), 4.70−5.00 (s, 7H, C-1 H of β-CD), 4.40−4.60 (m, 6H, O-6 H of β-CD), 3.00−4.00 (m, 42H, C-2, C-3, C-4, C-5, C-6 H of β-CD). ESI-MS *m/z* 1396.51 ($M + H^+$), 1418.64 ($M + Na^+$). FTICR-MS *m/z* 717.74 ($M + K^+ + H^+$), 1396.55 ($M + H^+$), 1416.02 ($2M + K^+ + H^+$), 1434.50 ($M + K^+$), 2114.18 ($3M + K^+ + H^+$). Elemental Anal. Calcd for $C_{57}H_{81}O_{35}N_5 \cdot 5H_2O$: C 46.06, H 6.17, N 4.71. Found: C 45.91, H 6.23, N 4.92.

Acknowledgment. We thank the 973 Program (2006CB932900) and NNSFC (Nos. 90306009, 20421202, and 20772062) for financial support. We also thank the reviewers for their valuable comments and suggestions regarding the revision.

Supporting Information Available: X-ray crystallographic data of **1** in CIF format (CCDC no. 662572), general experimental methods, ^{1}H NMR spectra of **1**−**4**, ESI spectra of **1** and **2**, TEM images of **2**, and the FTICR-MS spectrum of **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO800488F

(16) Eliadou, K.; Giastas, P.; Yannakopoulou, K.; Mavridis, I. M. *J. Org. Chem.* **2003**, *68*, 8550–8557.
(17) Huang, L.; Tonelli, A. E. *J. Macromol. Sci., Rev. Macromol. Chem. Phys.* **1998**, *C38*, 781–837.